CLAIMS

1. A compound of formual (I):

$$O \longrightarrow (CH_2)_n \longrightarrow O \longrightarrow (CH_2)_p CR^{1a}R^{2a} \longrightarrow Ar^2$$

$$Ar^1 \longrightarrow CHCH_2NHCR^1R^2(CH_2)_m$$

$$OH$$
(I)

or a salt, solvate, or physiologically functional derivative thereof, wherein:

Ar1 is a group selected from

wherein R⁴ represents hydrogen, halogen, -(CH₂)_qOR⁷, -NR⁷C(O)R⁸, -NR⁷SO₂R⁸, -SO₂NR⁷R⁸, -NR⁷R⁸, -OC(O)R⁹ or OC(O)NR⁷R⁸, and R³ represents hydrogen, halogen or C₁₋₄ alkyl;

or R⁴ represents –NHR¹⁰ and R³ and –NHR¹⁰ together form a 5- or 6- membered heterocyclic ring;

R⁵ represents hydrogen, halogen, -OR⁷ or -NR⁷R⁸;

R⁸ represents hydrogen, halogen, haloC₁₋₄alkyl, -OR⁷, -NR⁷R⁸, -OC(O)R⁹_or OC(O)NR⁷R⁸;

 R^7 and R^8 each independently represents hydrogen or C_{1-4} alkyl, or in the groups $-NR^7R^8$, $-SO_2NR^7R^8$ and $-OC(O)NR^7R^8$, R^7 and R^8 independently represent hydrogen or C_{1-4} alkyl or together with the nitrogen atom to which they are attached form a 5-, 6- or 7- membered nitrogen-containing ring,

 R^9 represents an aryl (eg phenyl or naphthyl) group which may be unsubstituted or substituted by one or more substituents selected from halogen, C_{1-4} alkyl, hydroxy, C_{1-4} alkoxy or halo C_{1-4} alkyl; and

g is zero or an integer from 1 to 4;

Ar² is a group:

$$R^{12}$$
 or R^{12} R^{11} R^{13}

wherein

 R^{11} is selected from hydrogen, $C_{1\text{-}6}$ alkyl, hydroxy, $C_{1\text{-}6}$ alkoxy, cyano, nitro, halo, $C_{1\text{-}6}\text{haloalkyl}, \quad XCO_2R^{16}, \quad -XC(O)NR^{15}R^{16}, \quad -XNR^{14}C(O)R^{15}, \quad -XNR^{14}C(O)NR^{15}R^{16}, \\ -XNR^{14}C(O)NC(O)NR^{15}R^{16}, \quad -XNR^{14}SO_2R^{15}, \quad -XSO_2NR^{17}R^{18}, \quad XSR^{14}, \quad XSOR^{14}, \quad XSO_2R^{14}, \\ -XNR^{15}R^{16}, \quad -XNR^{14}C(O)OR^{15}, \quad \text{or } XNR^{14}SO_2NR^{15}R^{16}, \\ \text{or } R^{11} \text{ is selected from } -X\text{-aryl, } -X\text{-hetaryl, or } -X\text{-(aryloxy), each optionally substituted by 1 or 2 groups independently selected from hydroxy, } C_{1\text{-}6}\text{alkoxy, halo, } C_{1\text{-}6}\text{alkyl, } C_{1\text{-}6}\text{haloalkyl, cyano, nitro, } CONR^{15}R^{16}, \\ \label{eq:constraints}$

-NR¹⁴C(O)R¹⁵, SR¹⁴, SOR¹⁴, -SO₂R¹⁴, -SO₂NR¹⁷R¹⁸, -CO₂R¹⁶, -NR¹⁵R¹⁶, or hetaryl optionally substituted by 1 or 2 groups independently selected from hydroxy, C_{1-6} alkoxy, halo, C_{1-6} alkyl, or C_{1-6} haloalkyl;

X is $-(CH_2)_r$ or C_{2-6} alkenylene;

r is an integer from 0 to 6, preferably 0 to 4;

 R^{14} and R^{15} are independently selected from hydrogen, $C_{1\text{-}6}$ alkyl, $C_{3\text{-}7}$ cycloalkyl, aryl, hetaryl, hetaryl($C_{1\text{-}6}$ alkyl)- and aryl($C_{1\text{-}6}$ alkyl)- and R^{14} and R^{15} are each independently optionally substituted by 1 or 2 groups independently selected from halo, $C_{1\text{-}6}$ alkyl, $C_{3\text{-}7}$ cycloalkyl, $C_{1\text{-}6}$ alkoxy, $C_{1\text{-}6}$ haloalkyl, $-NHC(O)(C_{1\text{-}6}$ alkyl), $-SO_2(C_{1\text{-}6}$ alkyl),

or R¹⁴ and R¹⁵, together with the nitrogen atom to which they are bonded, form a 5-, 6- or 7-membered nitrogen – containing ring;

or where R¹¹ is –XNR¹⁴C(O)NR¹⁵R¹⁶, R¹⁴ and R¹⁵ may, together with the -NC(O)N- portion of the group R¹ to which they are bonded, form a saturated or unsaturated ring, preferably a 5-, 6-, or 7- membered ring, for example an imidazolidine ring, such as imidazolidine-2,4-dione;

or where R^{11} is $-XNR^{14}C(O)OR^{15}$, R^{14} and R^{15} may, together with the -NC(O)O- portion of the group R^{11} to which they are bonded, form a saturated or unsaturated ring, preferably a 5-, 6-, or 7- membered ring, for example an oxazolidine ring, such as oxazolidine-2,4-dione;

 R^{16} is selected from hydrogen, C_{1-8} alkyl and C_{3-7} cycloalkyl;

or where R¹¹ is –XC(O)NR¹⁵R¹⁶ or –XNR¹⁴C(O)NR¹⁵R¹⁶, R¹⁵ and R¹⁶ may, together with the nitrogen to which they are bonded, form a 5-, 6-, or 7- membered nitrogen containing ring;

 R^{17} and R^{18} are independently selected from hydrogen, C_{1-6} alkyl, C_{3-7} cycloalkyl, aryl, hetaryl, hetaryl(C_{1-6} alkyl)- and aryl(C_{1-6} alkyl)-, or R^{17} and R^{18} , together with the nitrogen to which they are bonded, form a 5-, 6-, or 7- membered nitrogen containing ring;

and R¹⁷ and R¹⁸ are each optionally substituted by one or two groups independently selected from halo, C₁₋₆alkyl, and C₃₋₇cycloalkyl, C₁₋₆haloalkyl;

 R^{12} is selected from hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, halo, aryl, aryl(C_{1-6} alkyl)-, C_{1-6} haloalkoxy, and C_{1-6} haloalkyl;

 R^{13} is selected from hydrogen, hydroxy, C_{1-6} alkyl, C_{1-6} alkoxy, halo, aryl, ar<u>yl</u>(C_{1-6} alkyl)-, C_{1-6} haloalkoxy, and C_{1-6} haloalkyl;

 R^1 and R^2 are independently selected from hydrogen and C_{1-4} alkyl with the proviso that the total number of carbon atoms in R^1 and R^2 is not more than 4:

one of R^{1a} and R^{2a} is selected from hydrogen and C_{1-4} alkyl, and the other of R^{1a} and R^{2a} represents C_{1-4} alkyl;

m is an integer of from 1 to 3; n is an integer of from 1 to 4; and p is zero or an integer of from 1 to 3;

and ____ represents a single or double bond.

2. A compound of formula (I) as defined in claim 1, or a salt, solvate or physiologically functional derivative thereof, except that:

R^{1a} and R^{2a} each represent hydrogen;

and in the group Ar1, either:

 R^4 represents halogen, -(CH₂)_qOR⁷, -NR⁷C(O)R⁸, -NR⁷SO₂R⁸, -SO₂NR⁷R⁸, -NR⁷R⁸,

-OC(O)R 9 or OC(O)NR 7 R 8 , and R 3 represents hydrogen or C $_{1\text{--}4}$ alkyl;

or:

R⁴ represents –NHR¹⁰ and R³ and –NHR¹⁰ together form a 5- or 6- membered heterocyclic ring;

- 3. A compound of formula (I) according to either claim 1 or claim 2 wherein the group Ar^1 is selected from groups (a) and (b) as defined in claim 1.
- 4. A compound of formula (I) according to any of claims 1 to 3 wherein, in the group Ar², R¹¹ is selected from hydrogen, C₁₋₄alkyl, hydroxy, halo, -NR¹⁴C(O)NR¹⁵R¹⁶,

- -NR¹⁴SO₂R¹⁵ and XSO₂NR¹⁷R¹⁸ wherein R¹⁴ to R¹⁸ are as defined in claim 1.
- 5. A compound of formula (I) according to any of claims 1 to 3 wherein, in the group Ar^2 , R^{11} is selected from cyano, -CONR¹⁵R¹⁶, SR^{14} , SOR^{14} and SO_2R^{14} , wherein R^{14} , R^{15} and R^{16} are as defined in claim 1.
- 6. A compound of formula (I) according to any of claims 1 to 5 wherein R¹² and R¹³ each represent hydrogen.
- 7. A compound of formula (I) according to any of claims 1 to 3 wherein R^{11} represents hydrogen and R^{12} and R^{13} each represent halogen or C_{1-8} alkyl.
- 8. A compund of formula (I) according to any of claims 1 to 7 wherein R^1 and R^2 are both hydrogen.
- 9. A compound of formula (I) according to any of claims 1 to 8 wherein each of m and n is independently 1 or 2, and p is zero or 1.
- 10. A compound of formula (I) selected from:
- $4-((1R)-2-\{[2-((3R)-3-\{[(2,6-Dichlorobenzyl)oxy]methyl\}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;$
- 4-{(1*R*)-2-[(2-{(3*R*)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
- $4-{(1R)-2-[(2-{(3S)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino}-1-hydroxyethyl}-2-(hydroxymethyl)phenol;$
- 2-(Hydroxymethyl)-4- $\{(1R)$ -1-hydroxy-2- $[(2-\{(3R)$ -3-[(pyridin-3-ylmethoxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]ethyl}phenol;
- 4-((1R)-2-{[2-((3R)-3-{[(6-Chloropyridin-3-yl)methoxy]methyl}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
- 4-((1R)-2-{[2-((3R)-3-{[(2,6-Dichloropyridin-3-yl)methoxy]methyl}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
 - 4-{(1*R*)-2-[(2-{2-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)phenol;
 - $4-((1R)-2-\{[2-((3R)-3-\{[(5-Bromopyridin-3-yl)methoxy]methyl\}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino\}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;$

 $3-[({(2R)-7-[2-({(2R)-2-Hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl}amino)ethyl]-2,3-dihydro-1,4-benzodioxin-2-yl}methoxy)methyl]benzonitrile;$

- $3-[(((2R)-7-[2-(((2R)-2-Hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl]amino)ethyl]-2,3-dihydro-1,4-benzodioxin-2-yl}methoxy)methyl]benzamide;$
- 4-[(1*R*)-2-((2-[(3*R*)-3-({[3-(Cyclopentylthio)benzyl]oxy}methyl)-2,3-dihydro-1,4-benzodioxin-6-yl]ethyl}amino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol;
- 4-[(1R)-2-((2-[(3R)-3-({[3-(Cyclopentylsulfonyl)benzyl]oxy}methyl)-2,3-dihydro-1,4-benzodioxin-6-yl]ethyl}amino)-1-hydroxyethyl]-2-(hydroxymethyl)phenol;
- 2-(Hydroxymethyl)-4-{(1*R*)-1-hydroxy-2-[(2-{(3*R*)-3-[({5-[4-(methylsulfinyl)phenyl]pyridin-3-yl}methoxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]ethyl}phenol;
- $N-\{3-[((2R)-7-[2-((2R)-2-Hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl\}amino)ethyl]-2,3-dihydro-1,4-benzodioxin-2-yl}methoxy)methyl]phenyl}urea;$
- 4-((1R)-2-{[2-((3R)-3-{[(4-Chlorobenzyl)oxy]methyl}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;
- $4-((1R)-2-\{[2-((3R)-3-\{[(4-Fluorobenzyl)oxy]methyl\}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;$
- $4-((1R)-2-\{[2-((3R)-3-\{[(3,5-Dimethylbenzyl)oxy]methyl\}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;$
- 2-(Hydroxymethyl)-4- $\{(1R)$ -1-hydroxy-2- $[(2-\{(3R)$ -3-[(1-phenylethoxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]ethyl}phenol;
- $2-(Hydroxymethyl)-4-[(1R)-1-hydroxy-2-(\{2-[(3R)-3-(\{[3-(methylsulfonyl)benzyl]oxy\}methyl)-1-hydroxy-2-(\{2-[(3R)-3-(\{[3-(methylsulfonyl)benzyl]oxy\}methyl)-1-hydroxy-2-(\{2-[(3R)-3-(\{[3-(methylsulfonyl)benzyl]oxy\}methyl)-1-hydroxy-2-(\{2-[(3R)-3-(\{[3-(methylsulfonyl)benzyl]oxy\}methyl)-1-hydroxy-2-(\{[3-([(3R)-3-(\{[3-(methylsulfonyl)benzyl]oxy\}methyl)-1-hydroxy-2-(\{[3-([(3R)-3-(\{[3-([(3R)-([(3R)-3-([(3R)-3-([(3R)-3-([(3R)-([(3R)-3-([(3R)-3-([(3R)-3-([(3R)-3-([(3R)-([(3R)-([(3R)-([(3R)-([(3R)-([(3R)-([(3R)-([(3R)-([$
- 2,3-dihydro-1,4-benzodioxin-6-yl]ethyl}amino)ethyl]phenol;
- $4-((1R)-2-\{[2-((3R)-3-\{[3-(2,6-Dichlorophenyl)propoxy]methyl\}-2,3-dihydro-1,4-benzodioxin-6-yl)ethyl]amino}-1-hydroxyethyl)-2-(hydroxymethyl)phenol;$
- $3-[({(2R)-7-[2-({(2R)-2-Hydroxy-2-[4-hydroxy-3-(hydroxymethyl)phenyl]ethyl}amino)ethyl]-2,3-dihydro-1,4-benzodioxin-2-yl}methoxy)methyl]benzenesulfonamide;$
- 6-{2-[(2-{(3R)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-(hydroxymethyl)pyridin-3-ol;
- N-(5-{(1*R*)-2-[(2-{(3*R*)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-hydroxyphenyl)methanesulfonamide;
- $^4-{(1R)-2-(2-(3R)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-fluorophenol;$
- 4-{(1*R*)-2-[(2-{(3*R*)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-3-methylphenol;
- (1*R*)-1-(4-Amino-3,5-dichlorophenyl)-2-[(2-{(3*R*)-3-[(benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]ethanol;

5-{(1*R*)-2-[(2-{(3*R*)-3-[(Benzyloxy)methyl]-2,3-dihydro-1,4-benzodioxin-6-yl}ethyl)amino]-1-hydroxyethyl}-2-hydroxyphenylformamide;

or a salt, solvate or physiologically functional derivative thereof.

- 11. A method for the prophylaxis or treatment of a clinical condition in a mammal, such as a human, for which a selective β_2 -adrenoreceptor agonist is indicated, which comprises administration of a therapeutically effective amount of a compound of formula (I) according to any of claims 1 to 10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof.
- 12. A compound of formula (I) according to any of claims 1 to 10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof for use in medical therapy.
- 13. A pharmaceutical formulation comprising a compound of formula (I) according to any of claims 1 to 10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof, and a pharmaceutically acceptable carrier or excipient, and optionally one or more other therapeutic ingredients.
- 14. The use of a compound of formula (I) according to any of claims 1 to 10, or a pharmaceutically acceptable salt, solvate, or physiologically functional derivative thereof in the manufacture of a medicament for the prophylaxis or treatment of a clinical condition for which a selective β_2 -adrenoreceptor agonist is indicated.
- 15. A process for the preparation of a compound of formula (I), according to any of claims 1 to 10, or a salt, solvate, or physiologically functional derivative thereof, which comprises:
 - (a) deprotection of a protected intermediate, for example of formula (II).

$$Ar^{18} - CHCH_{2}NR^{23}CR^{1}R^{2}(CH_{2})_{m} - O-(CH_{2})_{p}CR^{18}R^{28} - Ar^{28}CR^{1}R^{2}(CH_{2})_{m}$$
(II)

or a salt or solvate thereof, wherein R¹, R², R^{1a}, R^{2a}, m, n, p and ____ are as defined for the compound of formula (I), Ar^{1a} represents an optionally protected form of Ar¹; Ar^{2a} represents an optionally protected form of Ar² and R²³ and R²⁴ are each independently either hydrogen or a protecting group, provided that the compound of formula (II) contains at least one protecting group;

(b) alkylation of an amine of formula

wherein Ar^{1a}, R²³ and R²⁴ are as defined for formula (II) with a compound of formula (XV):

$$LCR^{1}R^{2}(CH_{2})_{m} CR^{1a}R^{2a}Ar^{2a}$$

$$(CH_{2})_{n}O(CH_{2})_{p}CR^{1a}R^{2a}Ar^{2a}$$

$$(XV)$$

wherein $\underline{---}$, Ar^2 , R^1 , R^2 , R^{1a} , R^{2a} , m, n and p are as defined for the compound of formula (II) and L is a leaving group as defined for formula (IX);

followed by the following steps in any order:

- (i) optional removal of any protecting groups;
- (ii) optional separation of an enantiomer from a mixture of enantiomers;
- (iii) optional conversion of the product to a corresponding salt, solvate, or physiologically functional derivative thereof.